

WO 99/11780

PCT/DE98/02621

1/10

MSSAVLVTLLPD~~P~~SSSFREDAPRPPVPGEEGETPPCQPSVGKVQSTKPM~~P~~VSSNARRNED 60  
GLGEPEGRASPDSPLTRWTKSLH~~S~~LLGDQDGAYLFRTFLEREKCVD~~TLD~~F~~WFACNG~~FROM 120  
NLKDTKTLRVAKAIYKRYIENNSVVS~~K~~QLPATKTYIRDGIKKKQIGSVMF~~DQAQTEIQA~~ 180  
VMEENAYQVFLTS~~D~~IYLEYVRSGGENTAYMSNGGLGSLKVLCGYLPTLN~~EEE~~WTCA~~DLK~~ 240  
CKLSPTVVGLSSKTLRATASVRSTET~~A~~ENGFRSFKRSDPVNPYHVGSYV~~F~~APATSANDS 300  
ELSSDALTDDSMSMTDSSVDGVPPYRMGSKKQLQREMR~~H~~RSVKANGQVSLPHFPRTHRLPK 360  
EMTPVEPAFAELISRLEK~~L~~KLELESRHSLEERLQQIREDEEKEGSEQALSSRDGA~~VQ~~ 420  
EPLALLPSGSYEDPOTI~~L~~DDHLSRVLKTPGCQSPGVGRYS~~PRSRS~~PDHHHQHHHQCH 480  
TLLSTGGKLPPVAA~~C~~PLLGGKSFLTKQTTKHVHHYIHHAVPKTKEEIEA~~T~~QRVRCL 540  
CPGGTDYYCYSKCKSHPKA~~P~~EPLPGEQFCGSRGGTLPKRNAKGTEPGLALSARDGGMSSA 600  
AGGPQLPGEEGDRSQDVWQWMLSERQSKSKP~~H~~SAQSIRKSYS9LESARA1PGERVSR4HL 660  
LGASCHRSRVARAH~~P~~FTQDPAMPPLTPPN~~T~~LAQLEEA~~C~~RRLAEVSK9QKQRCCVASQQRD 720  
PNHSAAGQAGLSPFANPSLA~~P~~EDHKEPKKLASVHALQAS2LVV~~T~~YFFCGEEIPYREM1KA 780  
QSLTGHFKEQLSKKGNYRYYF~~K~~KASDEFACGAV~~EEI~~WDDETVLPMYEGRILCKVERID 840

D050500 "4554554550

Abb. 1

WO 99/11780

PCT/DE98/02621

2/10

CAGCCGTTCGCATGGATTCGGGCCACCCGGAGGGCGAGGCCGTCCGGCTCCCCAAAGG 60  
 AGAGCTTGTGTAAGAGAGGAGGCTCACATGAGCCCTGCTGACITAAGAGAGACCA 120  
 AGCCGATTGCTGAGAGGAACCTGAAGAAGAAAAAGGAGGAGGAOGGAAAAAGCAAAC 180  
 AAAATCCAACACTCAGTGAGACGCTCCCTCACCATGAGTAGCGCCGTTAGTQACTCT 240  
 CCTTCAGATCCCAGCAGCACTCCGCGAGGAATGCTCCGCGGCCCCGGTICGGGAGA 300  
 AGAAGGGAGACCCCACCGTGTAGCTAGTGAGGCAAGGTCCAGTCCACCAAACCTAI 360  
 GCCCGTTCTCTAAATGCTAAGCGGAATGAACATGGACTGGGGAGCCCCGAGGGCGGGC 420  
CTCCCCCGATTCCTCTTGAACCAGGTGCGACCAAGTCTTACACTCTTGTGGGTGACCA 480  
GGATGGTGACATACCTCTTCCGGACTTCTGGAGAGGGAGAAATGTGTGGATACGCTGGA 540  
CTTCTGGTTTGCTTGTAAATGGGTCAGGCAGATGAAACCTGAAGGATAACAAAACCTTGCG 600  
AGTGGCCAAAGCAATCTATAAGAGGTACATTGAGAACACAACAGCTGTCTCCAAGCAGCT 660  
GAAGCCCGCCACCAAGACCTACATAGAGATGGCATCAAGAACAAAGATCGGCTCGGT 720  
CATGTTGACCAAGGCACAGACCGAGATCCAGGCAGTGTGGAGGAAATGCCCTACCAAGGT 780  
GTTCCTGACTTCTGACATTACCTGGAATATGTGAGGAGTGGGGGGAAAACACAGCTIA 840  
 CATGAGTAACGGGGGACTGGGAGCCTAAAGGCTTATGTGGCTACCTCCCCACCTTGAA 900  
 TGAAGAAAGAGGAGTGGACGTGTCGGCACCTCAAGTGCAAACCTCACCCACCGTGGTGG 960  
 CTITGCCAGCAAAACTCTCCGGCCACCGCGAGTGTGAGATCCACCGAAACAGCTGAAAAA 1020  
 CGGATTCAAGGCTCTICAAGAGAACGACCCAGTCATCCCTAACGTTAGGTICCGGCTA 1080  
 TGTCCTTGACCAAGCCACCAACGCCAACAGCAGCGAGTTATCCAGCGACOCACTGACCGA 1140  
 CGATTCATGTCATGACGGACAGTAGCTAGATGGAGTCCCTCTTACCGCATGGGAG 1200  
 TAAGAAAACAGCTCCAGAGAGAGATGCAITCCAGTGTGAAGGCCAATGGCAAGTGTCTCT 1260  
ACCTCATTTCCGAGAACCCACCGCCCTGCCCAAGGAGATGACGCCGTGGAACCTGCTGC 1320  
CTTCGCCGCCAGCTCATCTCCAGGCTGGAGAAAACGAAACTGGACCTGGAAAGCCGCCA 1380  
TAGTCTGGAGGAGCGGCTGCAGCAGATCCGGGAGGATGAAGAAAAGGAGGGTCTGAGCA 1440  
GGCCCTGACCTCACGGATGGAGCACCGGCCAGCACCCCTGGCCCTCTTACCCCTCCG 1500  
CAGCTATGAAGAGGACCCACAAACATTGGACGACCACCTCTCCAGGGTCTCAAGAC 1560  
CCCCGGCTGTCATCTCTGGTGTGGTCGCTACAGCCACGGTCCCGCTCCCCCGACCA 1620  
CCACCAACAGCACCAACACATCAGCAGTGTACCCCTTTCAGTGGAGCTGGGCAAGCT 1680  
GCCCCCGTGGCTGCTTGGCCCTCTGGAGGCAAGAGCTCCITGACCAACAGACGAC 1740  
GAAGCACGTTACCAACCACTACATCCACCAACGCCAGCGCTCCAAAGACCAAGGAGGAGAT 1800  
CGAGGCAGAACGCCACACAGAGAGTCCGCTGCCCTGTCTGGGGAAACAGATTATIG 1860  
CTACTCCAATGCAAAGCCACCCGAAGGCTCCAGAGCCCTGGGAGCAGTTTG 1920  
TGGCAGCAGGGTGGTACCTGCCAAAACGGAATGCAAAGGGCACCGAACCGGGCTTGC 1980  
ACTGTCGGCCAGGGATGGAGGGATGTCAGTGTGAGCGGGGGGGGGGGAGCTTCTGGGG 2040  
AGAAGGAGACCGGTACAGGATGTCGGAGTGGAGTGTGGAGAGTGAGCGGCAGAGCAA 2100  
GTCCAAGCCCATACTGCCCCAAAGCATAAGAAAGAGCTACCCATGGAGTGTGCCGTGC 2160  
GGCCCCAGGAAGACGAGTCAGCCGGCACCATCTGTCGGGCCAGCGGACACTCCCGCTC 2220  
AGTGGCCCGGGCTACCCATTACCCAGGACCTGCAATGCCCTCCCTAACCCACCCAA 2280  
CACTTGGCACAGCTAGAGGAAGCCCTGCCAGGCTGGAGGGTICGAAGCCCCAGAA 2340  
GCAGCGGTGCGTGGCCAGTCAGCAGAGGGACAGGAACCACTGGCTGGCTGGTCAGGC 2400  
AGGAGCCTCACCTTCGCCAACCCAAGCTGGCTCCAGAAGATCACAAAGAGCCAAAGAA 2460  
ACTGGCAAGTGTCCACGCGCTCCAGGCCAGTGAGCTGGTGTACCTACTTTCTGTGG 2520  
AGAAAGAAATTCTACACAGGAGATGCTGAAGGCTCAAAGCTTGACCCCTGGGCCACCTGAA 2580  
GGAGCAGCTCACCAAAAGGAAATTACAGGTATTATTCAGAAGAAGGCGAGTGACGAATT 2640  
TGCCTGCGGAGCAGTTTGAGGAGATCTGGGACGACGAGACAGTGCTCCCATGTACGA 2700  
AGGCAGGATCTGGGCAAGTGGAGAGGATGACTGAGCTTGGCCCTCAGGGTGCACCA 2760  
CCTGGGCAAGCACCTC90CGTGCACCATGGAGCCGAAGCCCAGAGACCCCTGCTCAGGCC 2820  
TACGC 2825

Abb. 2

WO 99/11780

PCT/DE98/02621

3/10

215	ATG	AGT	AGC	GCC	GTG	TTA	GTG	ACT
1	M	S	S	A	V	L	V	T
CTC	CTT	CCA	GAT	CCC	AGC	AGC	AGC	TTC
L	L	P	D	P	S	S	S	F
CGC	GAG	GAT	GCT	CCG	CGG	CCC	CCG	GTT
R	E	D	A	P	R	P	P	V
CCG	GGA	GAA	GAA	GGG	GAG	ACC	CCA	CCG
P	G	E	E	G	E	T	P	P
TGT	CAG	CCT	AGT	GTG	GGC	AAG	GTC	CAG
C	Q	P	S	V	G	K	V	Q
TCC	ACC	AAA	CCT	ATG	CCC	GTT	TCC	TCT
S	T	K	P	M	P	V	S	S
AAT	GCT	AGG	CGG	AAT	GAA	GAT	GGA	CTG
N	A	R	R	N	E	D	G	L
GGG	GAG	CCC	GAG	GGG	CGG	GCC	TCC	CCC
G	E	P	E	G	R	A	S	P
GAT	TCC	CCT	TTG	ACC	AGG	TGG	ACC	AAG
D	S	P	L	T	R	<u>W</u>	T	<u>K</u>
TCT	TTA	CAC	TCC	TTG	TTG	GGT	GAC	CAG
<u>S</u>	<u>L</u>	<u>H</u>	<u>S</u>	<u>L</u>	<u>L</u>	<u>G</u>	<u>D</u>	<u>Q</u>
GAT	GGT	GCA	TAC	CTC	TTC	CGG	ACT	TTC
<u>D</u>	<u>G</u>	<u>A</u>	<u>Y</u>	<u>L</u>	<u>F</u>	<u>R</u>	<u>T</u>	<u>F</u>
CTG	GAG	AGG	GAG	AAA	TGT	GTG	GAT	ACG
<u>L</u>	<u>E</u>	<u>R</u>	<u>E</u>	<u>K</u>	<u>C</u>	<u>V</u>	<u>D</u>	<u>T</u>
CTG	GAC	TTC	TGG	TTT	GCT	TGT	AAT	GGG
<u>L</u>	<u>D</u>	<u>F</u>	<u>W</u>	<u>F</u>	<u>A</u>	<u>C</u>	<u>N</u>	<u>G</u>

Abb. 3

WO 99/11780

PCT/DE98/02621

4/10

TTC	AGG	CAG	ATG	AAC	CTG	AAG	GAT	ACC
<u>F</u>	<u>R</u>	<u>Q</u>	<u>M</u>	<u>N</u>	<u>L</u>	<u>K</u>	<u>D</u>	<u>T</u>
AAA	ACT	TTG	CGA	GTG	GCC	AAA	GCA	ATC
<u>K</u>	<u>T</u>	<u>L</u>	<u>R</u>	<u>V</u>	<u>A</u>	<u>K</u>	<u>A</u>	<u>I</u>
TAT	AAG	AGG	TAC	ATT	GAG	AAC	AAC	AGC
<u>Y</u>	<u>K</u>	<u>R</u>	<u>Y</u>	<u>I</u>	<u>E</u>	<u>N</u>	<u>N</u>	<u>S</u>
GTT	GTC	TCC	AAG	CAG	CTG	AAG	CCC	GCC
<u>V</u>	<u>V</u>	<u>S</u>	<u>K</u>	<u>Q</u>	<u>L</u>	<u>K</u>	<u>P</u>	<u>A</u>
ACC	AAG	ACC	TAC	ATA	CGA	GAT	GGC	ATC
<u>T</u>	<u>K</u>	<u>T</u>	<u>Y</u>	<u>I</u>	<u>R</u>	<u>D</u>	<u>G</u>	<u>I</u>
AAG	AAG	CAA	CAG	ATC	GGC	TCG	GTC	ATG
<u>K</u>	<u>K</u>	<u>O</u>	<u>O</u>	<u>I</u>	<u>G</u>	<u>S</u>	<u>V</u>	<u>M</u>
TTT	GAC	CAG	GCA	CAG	ACC	GAG	ATC	CAG
<u>F</u>	<u>D</u>	<u>Q</u>	<u>A</u>	<u>Q</u>	<u>T</u>	<u>E</u>	<u>I</u>	<u>Q</u>
GCA	GTG	ATG	GAG	GAA	AAT	GCC	TAC	CAG
<u>A</u>	<u>V</u>	<u>M</u>	<u>E</u>	<u>E</u>	<u>N</u>	<u>A</u>	<u>Y</u>	<u>Q</u>
GTG	TTC	TTG	ACT	TCT	GAC	ATT	TAC	CTG
<u>V</u>	<u>F</u>	<u>L</u>	<u>T</u>	<u>S</u>	<u>D</u>	<u>I</u>	<u>Y</u>	<u>L</u>
GAA	TAT	GTG	AGG	AGT	GGG	GGG	GAA	AAC
<u>E</u>	<u>Y</u>	<u>V</u>	<u>R</u>	<u>S</u>	<u>G</u>	<u>G</u>	<u>E</u>	<u>N</u>
ACA	GCT	TAC	ATG	AGT	AAC	GGG	GGA	CTG
<u>T</u>	<u>A</u>	<u>Y</u>	<u>M</u>	<u>S</u>	<u>N</u>	<u>G</u>	<u>G</u>	<u>L</u>
GGG	AGC	CTA	AAG	GTC	TTA	TGT	GGC	TAC
<u>G</u>	<u>S</u>	<u>L</u>	<u>K</u>	<u>V</u>	<u>L</u>	<u>C</u>	<u>G</u>	<u>Y</u>
CTC	CCC	ACC	TTG	AAT	GAA	GAA	GAG	GAG
<u>L</u>	<u>P</u>	<u>T</u>	<u>L</u>	<u>N</u>	<u>E</u>	<u>E</u>	<u>E</u>	<u>E</u>

Abb. 3

WO 99/11780

PCT/DE98/02621

5/10

TGG	ACG	TGT	GCC	GAC	CTC	AAG	TGC	AAA
W	T	C	A	D	L	K	C	K
CTC	TCA	CCC	ACC	GTG	GTT	GGC	TTG	TCC
L	S	P	T	V	V	G	L	S
AGC	AAA	ACT	CTT	CGG	GCC	ACC	GCG	AGT
S	K	T	L	R	A	T	A	S
GTG	AGA	TCC	ACG	GAA	ACA	GCT	GAA	AAC
V	R	S	T	E	T	A	E	N
GGA	TTC	AGG	TCC	TTC	AAG	AGA	AGC	GAC
G	F	R	S	F	K	R	S	D
CCA	GTC	AAT	CCT	TAT	CAC	GTA	GGT	TCC
P	V	N	P	Y	H	V	G	S
GGC	TAT	GTC	TTT	GCA	CCA	GCC	ACC	AGC
G	Y	V	F	A	P	A	T	S
GCC	AAC	GAC	AGC	GAG	TTA	TCC	AGC	GAC
A	N	D	S	E	L	S	S	D
GCA	CTG	ACC	GAC	GAT	TCC	ATG	TCC	ATG
A	L	T	D	D	S	M	S	M
ACG	GAC	AGT	AGC	GTA	GAT	GGA	GTC	CCT
T	D	S	S	V	D	G	V	P
CCT	TAC	CGC	ATG	GGG	AGT	AAG	AAA	CAG
P	Y	R	M	G	S	K	K	Q
CTC	CAG	AGA	GAG	ATG	CAT	CGC	AGT	GTG
L	Q	R	E	M	H	R	S	V
AAG	GCC	AAT	GGC	CAA	GTG	TCT	CTA	CCT
K	A	N	G	Q	V	S	L	P
CAT	TTT	CCG	AGA	ACC	CAC	CGC	CTG	CCC
H	F	P	R	T	H	R	L	P

Abb. 3

WO 99/11780

PCT/DE98/02621

6/10

AAG GAG ATG ACG CCT GTG GAA CCT GCT  
K E M T P V E P A

GCC TTC GCC GCC GAG CTC ATC TCC AGG  
A F A A E L I S R

CTG GAG AAA CTG AAA CTG GAG CTG GAA  
L E K L K L E L E

AGC CGC CAT AGT CTG GAG GAG CGG CTG  
S R H S L E E R L

CAG CAG ATC CGG GAG GAT GAA GAA AAG  
Q Q I R E D E E K

GAG GGG TCT GAG CAG GCC CTG AGC TCA  
E G S E O A L S S

CGG GAT GGA GCA CCG GTC CAG CAC CCC  
R D G A P V O H P

CTG GCC CTC CTA CCC TCC GGC AGC TAT  
L A L L P S G S Y

GAA GAG GAC CCA CAA ACC ATT TTG GAC  
E E D P Q T I L D

GAC CAC CTC TCC AGG GTC CTC AAG ACC  
D H L S R V L K T

CCC GGC TGT CAA TCC CCT GGT GTG GGT  
P G C Q S P G V G

CGC TAC AGC CCA CGG TCC CGC TCC CCC  
R Y S P R S R S P

GAC CAC CAC CAC CAG CAC CAC CAC CAT  
D H H H Q H H H H

Abb. 3

WO 99/11780

PCT/DE98/02621

7/10

CAG	CAG	TGT	CAT	ACC	CTT	CTT	TCG	ACT
Q	Q	C	H	T	L	L	S	T
GGG	GGC	AAG	CTG	CCC	CCC	GTG	GCT	GCT
G	G	K	L	P	P	V	A	A
TGC	CCC	CTC	CTT	GGA	GGC	AAG	AGC	TTC
C	P	L	L	G	G	K	S	F
CTG	ACC	AAA	CAG	ACG	ACG	AAG	CAC	GTT
L	T	K	Q	T	T	K	H	V
CAC	CAC	CAC	TAC	ATC	CAC	CAC	CAC	GCC
H	H	H	Y	I	H	H	H	A
GTC	CCC	AAG	ACC	AAG	GAG	GAG	ATC	GAG
V	P	K	T	K	E	E	I	E
GCA	GAA	GCC	ACA	CAG	AGA	GTC	CGC	TGC
A	E	A	T	Q	R	V	R	C
CTC	TGT	CCT	GGG	GGA	ACA	GAT	TAT	TAT
L	C	P	G	G	T	D	Y	Y
TGC	TAC	TCC	AAA	TGC	AAA	AGC	CAC	CCG
C	Y	S	K	C	K	S	H	P
AAG	GCT	CCA	GAG	CCC	CTG	CCT	GGG	GAG
K	A	P	E	P	L	P	G	E
CAG	TTT	TGT	GGC	AGC	AGA	GGT	GGT	ACC
Q	F	C	G	S	R	G	G	T
TTG	CCA	AAA	CGG	AAT	GCA	AAG	GGC	ACC
L	P	K	R	N	A	K	G	T
GAA	CCG	GGT	CTT	GCA	CTG	TCG	GCC	AGG
E	P	G	L	A	L	S	A	R
GAT	GGA	GGG	ATG	TCC	AGT	GCA	GCG	GGG
D	G	G	M	S	S	A	A	G

Ahh. 3

WO 99/11780

PCT/DE98/02621

8/10

GGC	CCC	CAG	CTT	CCT	GGG	GAA	GAA	GGA
G	P	Q	L	P	G	E	E	G
GAC	CGG	TCA	CAG	GAT	GTC	TGG	CAG	TGG
D	R	S	Q	D	V	W	Q	W
ATG	TTG	GAG	AGT	GAG	CGG	CAG	AGC	AAG
M	L	E	S	E	R	Q	S	K
TCC	AAG	CCC	CAT	AGT	GCC	CAA	AGC	ATA
S	K	P	H	S	A	Q	S	I
AGA	AAG	AGC	TAC	CCA	TTG	GAG	TCT	GCC
R	K	S	Y	P	L	E	S	A
CGT	GCG	GCC	CCA	GGA	GAA	CGA	GTC	AGC
R	A	A	P	G	E	R	V	S
CGG	CAC	CAT	CTG	TTG	GGG	GCC	AGC	GGA
R	H	H	L	L	G	A	S	G
CAC	TCC	CGC	TCA	GTG	GCC	CGG	GCT	CAC
H	S	R	S	V	A	R	A	H
CCA	TTT	ACC	CAG	GAC	CCT	GCA	ATG	CCT
P	F	T	Q	D	P	A	M	P
CCC	CTT	ACC	CCA	CCC	AAC	ACT	TTG	GCA
P	L	T	P	P	N	T	L	A
CAG	CTA	GAG	GAA	GCC	TGC	CGC	AGG	CTG
Q	L	E	E	A	C	R	R	L
GCA	GAG	GTG	TCG	AAG	CCC	CAG	AAG	CAG
A	E	V	S	K	P	Q	K	Q
CGG	TGC	TGC	GTG	GCC	AGT	CAG	CAG	AGG
R	C	C	V	A	S	Q	Q	R

Abb. 3

WO 99/11780

PCT/DE98/02621

9/10

GAC	AGG	AAC	CAC	TCG	GCT	GCT	GGT	CAG
D	R	N	H	S	A	A	G	Q
GCA	GGA	GCC	TCA	CCC	TTC	GCC	AAC	CCA
A	G	A	S	P	F	A	N	P
AGC	CTG	GCT	CCA	GAA	GAT	CAC	AAA	GAG
S	L	A	P	E	D	H	K	E
CCA	AAG	AAA	CTG	GCA	AGT	GTC	CAC	GCG
P	K	K	L	A	S	V	H	A
CTC	CAG	GCC	AGT	GAG	CTG	GTT	GTC	ACC
L	Q	A	S	E	L	V	V	T
TAC	TTT	TTC	TGT	GGA	GAA	GAA	ATT	CCA
Y	F	F	C	G	E	E	I	P
TAC	AGG	AGG	ATG	CTG	AAG	GCT	CAA	AGC
Y	R	R	M	L	K	A	Q	S
TTG	ACC	CTG	GGC	CAC	TTC	AAG	GAG	CAG
L	T	L	G	H	F	K	E	Q
CTC	AGC	AAA	AAG	GGA	AAT	TAC	AGG	TAT
L	S	K	K	G	N	Y	R	Y
TAT	TTC	AAG	AAG	GCG	AGT	GAC	GAA	TTT
Y	F	K	K	A	S	D	E	F
GCC	TGC	GGA	GCA	GTT	TTT	GAG	GAG	ATC
A	C	G	A	V	F	E	E	I
TGG	GAC	GAC	GAG	ACA	GTG	CTC	CCC	ATG
W	D	D	E	T	V	L	P	M
TAC	GAA	GGC	AGG	ATC	CTG	GGC	AAA	GTG
Y	E	G	R	I	L	G	K	V
GAG	AGG	ATC	GAC	TGA	2737			
E	R	I	D	Stop				

Abb. 3

WO 99/11780

PCT/DE98/02621

10/10

**Conductin  
Konstrukte**

**Interaktion mit**

**Abbau von  $\beta$ -Catenin  
In SW480 Zellen**

$\beta$ -Catenin	APC #1	APC #2	GSK3 $\beta$
220	6	9	18
490	0	0	n.d.
1060	0	0	670
0	190	260	0
0	110	250	84
0	390	390	0

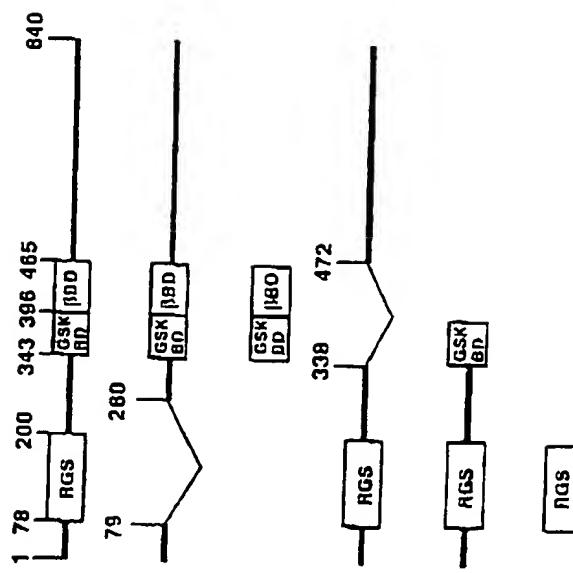


Abb. 4